UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/773,229	02/09/2004	Ronald Mathison	024916-013	4016

21839 7590 04/06/2005

BURNS DOANE SWECKER & MATHIS L L P
POST OFFICE BOX 1404
ALEXANDRIA, VA 22313-1404

EXAMINER	
GUPTA, ANISH	
ART UNIT	**PAPER NUMBER**
1654	

DATE MAILED: 04/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/773,229	MATHISON ET AL.	
	Examiner	Art Unit	
	Anish Gupta	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 21-41 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 21-41 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

HL

DETAILED ACTION

1. The preliminary amendment, filed 2-09-04, is acknowledged. Claims 1-20 were cancelled and claims 21-41 were added. Claims 21-41 are pending in this application.

Claim Rejections - 35 USC § 112

First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 21-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of inflammation with the peptide FEG and those specific tri-peptides claimed in US 6586403, does not reasonably provide enablement for any peptide corresponding to the formula R1-X1-X2-R2 for the same purpose or prevent inflammatory reactions or prevent infiltration of neutrophils into an inflammatory site. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to enable the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above

factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The invention are drawn to peptides that are effective in "preventing and/or treating inflammation, anaphylactic reactions, including anaphylactic shock, endotoxic reactions including endotoxic shosck, and SIRS."

(2) The state of the prior art

The art has not developed with respect to the peptide of the formula R1-X1-X2-R2 and prevention of anaphylactic reactions using such peptides.

(3) The relative skill of those in the art

The relative skill of the those in the art is high.

(4) The predictability or unpredictability of the art

As with all peptides, activity is based on the 3-dimensional structure of the peptide. That is, the peptide has to have the proper structure to recognize the specific receptor for the peptide to be active. It is known in the art that the three dimensional structure of the peptide cannot be based on structure alone. For example, in peptide chemistry Ngo et al. teach that for proteins and peptides, a " 'Direct' approach to structure prediction, that of directly simulating the folding process, is not yet possible because contemporary hardware falls eight to nine orders of magnitude short of the task." (see page 493 in Ngo et al.) Accordingly, it is not known if an efficient algorithm for

predicting the structure exist for a protein or peptide from its amino acid alone (see page 492 in Ngo et al.). Thus, activity of a given peptide can not be based on its structure alone. Similarly, the Rudinger article (see the conclusions in particular) states "The significance of particular amino acids or sequences for different aspects of biological activity cannot be predicted a priori but must be determined from the case to case by painstaking experimental study."

Furthermore, prevention is normally defined as to keep from happening or arising again. Prevention of inflammation in Rheumatoid Arthritis, for example, is unknown. The Merck Manual states that corticosteroids suppress inflammation for the longest period but do not completely "prevent" the inflammation (see page 1311). Inflammatory reactions and inflammation reoccur often in Rheumatoid Arthritis and need to be treated when they do occur. Similarly, in inflammatory bowl disease, prevention of inflammation is difficult to achieve. For Crohn's disease, a nonspecific chronic transmural inflammatory disease, the Merck Manual states that no specific therapy is known (see p. 833). Sulfazalazine therapy is useful in suppressing low grade inflammation but is less effective in sever acute exacerbations. Further, it is not been helpful in preventing postoperative recurrence (see page 833). Corticosteroid therapy only helps to reduce abdominal pain but not prevent it. In colitis, relapse is often observed and the symptoms are exceptionally stubborn and refractory (see page 837). Thus, prevention of inflammation or inflammatory reactions are difficult to achieve in inflammatory disorders.

(5) The breadth of the claims

The broadest claims are open to peptides of the formula R1-X1-X2-R2, where R1 is an amino acid sequence of three amino acids or NH2, X1 is an aromatic amino acid, X2 is any amino acid and R2

is a peptide up to three amino acids which are aliphatic amino acid residues. The claims are drawn to using these peptides for "treating or preventing an inflammatory reaction in a mammal" and "reducing or preventing the infiltration of neutrophils into a inflammatory site."

(6) The amount of direction or guidance presented and (7) The presence or absence of working examples

The specification does provide guidance as the reducing and treating effects on anaphylactic reactions with the peptide FEG. However, the specification fails to adequately provide ample guidance that any peptide corresponding to the formula R1-X1-X2-R2 will be effective in treating, reducing or preventing anaphylactic reactions. The example given in utilize a singe peptide corresponding to the sequence FEG. However, the claims are open to much broader sequences that may not even have conservative substitutions corresponding to FEG. It has been established in the art that one can not readily determine the effects of substitutions of amino acids to the native sequence based on structure alone. Again, Ngo et al. teach that for proteins and peptides, a " 'Direct' approach to structure prediction, that of directly simulating the folding process, is not yet possible because contemporary hardware falls eight to nine orders of magnitude short of the task." (see page 493 in Ngo et al.) Accordingly, it is not known if an efficient algorithm for predicting the structure exist for a protein or peptide from its amino acid alone (see page 492 in Ngo et al.). Thus, activity of a given peptide can not be based on its structure alone. Similarly, the Rudinger article (see the conclusions in particular) states "The significance of particular amino acids or sequences for different aspects of biological activity cannot be predicted a priori but must be determined from the case to case by painstaking experimental study."

Furthermore, the specification completely fails to disclose prevention of inflammation in Rheumatoid Arthriris or inflammatory bowel disease. As indicated above, prevention of inflammation or inflammatory reactions are difficult to achieve in inflammatory disorders. The specification fails to provide any guidance, except for broad allegation, that the peptides are effective in preventing inflammatory response.

The Board of Appeals has held *Ex parte Sudilovsky*, where it was held that the disclosure was non-enabling since:

> "[t]he specification, though highly detailed, is devoted solely to a description of compounds stated to be known ACE inhibitors. The remainder of the specification is directed to how to make tablets and solutions for injection. Any disclosure regarding utility is confined to broad allegations and suggestions without substantiating working example. As stated in *In re Glass*, 492 F.2d 1228, 181 USPQ 31, 35 (CCPA 1974), 'the strong feeling one gets from reading the entire specification is that either appellant did not have possession of the details of a single operative process or, if he did, he chose not to divulge them.'"

Ex parte Sudilovsky, 21 U.S.P.Q2d 1702 (BPAI 1991). Similarly, the disclosure of the instant application, with regard to the peptide corresponding to the formula R1-X1-X2-R2 and prevention of anaphylactic reactions, is confined to broad allegations and suggestions without substantiating working examples. Although working examples are not necessary in the specification, lack of a working example, however, is a factor to be considered, especially in a case involving an unpredictable and undeveloped art. When a patent applicant chooses to forego exemplification and bases utility on broad terminology and general allegations, he runs the risk that unless one with ordinary skill in the art would accept the allegations as obviously valid and correct, the examiner may, properly, ask for evidence to substantiate them. *In re Novak*, 306 F.2d 924, 134 USPQ 335 (CCPA 1962) 4; *In re Fouche*, 439 F.2d 1237, 169 USPQ 429 (CCPA 1971). In this case, the disclosure has not provided evidence of record of a representative set of compound corresponding

the formula and still possessing the claimed activity . Thus, given the unpredictability o f the art, undue experimentation would be required to practice the claimed invention.

(8) The quantity of experimentation necessary

Since, the art indicates a level of unpredictability in determining activity of a peptide based on structure alone one would be burdened with undue experimentation do practice the claimed invention for the reasons stated above.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 21-41 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-32 of U.S. Patent No. 6,586,403. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons.

The claims are drawn to using these peptides for "treating or preventing an inflammatory reaction in a mammal" and "reducing or preventing the infiltration of neutrophils into a inflammatory site" using peptides of the formula R1-X1-X2-R2.

The US Patent claims a method for modulating inflammatory reactions by administering a peptide of the formula X1-R1-R2-R3-Y (see claim 17). Note that the definitions of the Markush groups claimed in the US Patent encompass the peptides of the claimed invention. The US Patent claims the peptide phe-Glu-sarcosine, Dphe-Dglu-gly and phe-glu-gly when X is H, R1 is D phe or phe, R2 is Dglu or glu, and R3 is gly or sarcosine (see claim 1). These peptide are the same peptides that are claimed in claims 29-30 of the instant application. Furthermore, the US patent claims that the reaction involves inflammation of the gastrointestinal tract (see claim 28 of the US Patent). This renders obvious the inflammatory bowel disease of the instant claim 31. It would have been obvious, therefore, to make the tri-peptides claimed in the US patent and use them to treat inflammatory reactions because the US Patent claims that the tri-peptides, for example phe-Glu-sarcosine, Dphe-Dglu-gly and phe-glu-gly, are effective in treating inflammatory reactions when administered at a dosage of .1 to 1000 μg/kg.

As for the claims with regards to infiltration of neutrophils, since the US patent claims gastrointestinal inflammation can be treating using the tripeptides, it would have been obvious to administer the peptides to an individual suffering from colitis or Crohn's disease. Once administered to these patients, reduction of neutrophils would have necessarily been achieved since neutrophils are involved in the inflammatory response of inflammatory bowl syndrome.

Different Inventors, Common Assignee, Obvious Inventions, No Evidence of Common Ownership at Time of Invention

Claims 21-41are directed to an invention not patentably distinct from claims 1-15, 17, 25, and 28 of commonly assigned US 6,586,403. Specifically, The US Patent claims a method for modulating inflammatory reactions by administering a peptide of the formula X1-R1-R2-R3-Y (see claim 17).

Note that the definitions of the Markush groups claimed in the US Patent encompass the peptides of the claimed invention. The US Patent claims the peptide phe-Glu-sarcosine, Dphe-Dglu-gly and phe-glu-gly when X is H, R1 is D phe or phe, R2 is Dglu or glu, and R3 is gly or sarcosine (see claim 1). These peptide are the same peptides that are claimed in claims 29-30 of the instant application. Furthermore, the US patent claims that the reaction involves inflammation of the gastrointestinal tract (see claim 28 of the US Patent). This renders obvious the inflammatory bowel disease of the instant claim 31. It would have been obvious, therefore, to make the tri-peptides claimed in the US patent and use them to treat inflammatory reactions because the US Patent claims that the tri-peptides, for example phe-Glu-sarcosine, Dphe-Dglu-gly and phe-glu-gly, are effective in treating inflammatory reactions when administered at a dosage of .1 to 1000 μg/kg.

As for the claims with regards to infiltration of neutrophils, since the US patent claims gastrointestinal inflammation can be treating using the tripeptides, it would have been obvious to administer the peptides to an individual suffering from colitis or Crohn's disease. Once administered to these patients, reduction of neutrophils would have necessarily been achieved since neutrophils are involved in the inflammatory response of inflammatory bowl syndrome.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned US 6586403, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(e), (f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee can, under 35 U.S.C. 103(c) and 37 CFR 1.78(c), either show that the conflicting inventions were commonly

owned at the time the invention in this application was made, or name the prior inventor of the conflicting subject matter.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

3. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (571)272-0965. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can normally be reached on (571) 272-0974. The fax phone number of this group is (571)-273-8300.

3/28/08

Anish Gupta
Patent Examiner